

## **REMARKS**

Applicants filed the Application on August 24<sup>th</sup>, 1999. A Request for Continued Examination was mailed on October 30, 2003. The First Office Action was mailed on March 31<sup>st</sup>, 2004 with Claims 51 and 60-78 pending. Claims 51, 60-63, 70-72, and 74-78 are amended. New claims 79-292 are hereby added. Claim 79 is supported by the specification at page 13. Claims 80-292 are supported by Figure 2 and simply provide permutations of the sequence originally claimed generically in claim 60. No new matter is added by this amendment.

### **Drawings:**

Please amend Figure 9's Y-axis description from "KEPAN" to "KCPM". Please also amend Figure 2's title to read "Alignment of HSP47 with HLA/IL-12 $\beta$  Chains". These were unintentional errors by the draftsman. Applicants have not submitted color drawings. Applicants hereby submit for the Examiner's approval substitute figures for Figure 2 and 9 and respectfully request that the substituted drawings replace original Figures 2 and 9.

### **Specification:**

Please find enclosed a substituted specification incorporating all previous amendments made to the specification for the Examiner's convenience. No new matter was added to the specification. Future references to line numbers and pages reference this specification.

### **Claims:**

### **Informalities:**

Please amend “In the Claims” to “What is Claimed is” as originally presented. In our last response, “In the Claims” was not intended to be a change to the language of the application; it was a section header for the amendment and new claims in the response.

Rejections Under 35 U.S.C. § 112, first paragraph--Enablement

The Examiner has rejected claims 60-78 under 35 U.S.C. § 112, first paragraph as “containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record first set forth in the paper mailed 7/17/01 and reiterated in the paper mailed 10/02/02.” The Examiner has admitted, however, that species drawn to SEQ ID NOS: 3 and 6 are enabled.

Applicants respectfully disagree with the Examiner with respect to this rejection. As per the discussion at the interview of April 22, 2004, “the scope of the required enablement varies inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species is not required. A single embodiment may provide broad enablement in cases involving predictable factors.” *See In re Vickers*, 141 F.2d 522 (CCPA 1944) and MPEP 2164.04. Applicants respectfully argue that the instant case involves “predictable factors” that would provide broad enablement. With respect to claims that call for percent identities of peptide sequences, these percentages were based on the algorithm used in BLAST searching. At the time of filing, peptide synthesis was well known to those skilled in the art and the ability to identify the % of identity between similar peptide sequences using the algorithms provided by BLAST searches was known for greater than two decades. *See Atschul et al.*, *Methods in Enzymology*, 266:460-480 (1996) (a copy of which is enclosed for your convenience and cited on the enclosed Supplemental IDS) and the specification at pages 12-13. The quantity of

experimentation required to identify a peptide sequence with the requisite percent identity would be small and the methods to test whether the peptide of interest would function to protect cells, organs or tissues from immune-mediate damage is provided by the specification (*see* Examples 1, 3, 4, and 9). Additionally, Figure 2, for example, provides for a great many of the possible peptide sequences that embody the claims. Claims 80–292 are newly added and are drawn to these peptide sequences as provided by Figure 2.

The Examiner further states that, “none of the mutated or substituted forms of Hsp47 disclosed in the specification have been shown to function in the method of the instant claims,” and that “a lack of contradiction in the literature does not in itself comprise sufficient enablement for the method of the instant claims.”

Applicants respectfully disagree. As discussed during the interview, the data demonstrate that cells, organs or tissues are protected. Applicants would like to particularly point out some non-limiting examples in the specification which demonstrate that the mutated or substituted forms of Hsp47 disclosed in the specification does function in the methods of the instant claims: Figures 2, 9, 11, 12, 13, 15, page 27, page 55, and page 68 of the specification. According to MPEP 2164.01(b), “[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. § 112 is satisfied.” Applicants respectfully point out that at least two species identified as SEQ ID NOS: 3 and 6 are enabled as admitted by the Examiner. Therefore, the specification does in fact provide working embodiments of the claims. For the foregoing reasons, Applicant respectfully requests that the Examiner withdraw this rejection.

Rejections Under 35 U.S.C. § 112, first paragraph—New Matter

The Examiner has rejected claims 70-72 and 74-78 as rejected under 35 U.S.C. § 112, first paragraph, “as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.”

Applicants respectfully disagree with the Examiner, however, Applicants will amend claims 70-72 as per the suggestions of the Examiner at the interview. In complying with the Examiner’s suggestions, Applicants believe the claims as newly amended are in proper form for allowance.

Claim 74 is amended to reflect 4 out of 9 amino acids being substituted or omitted as supported in the specification by at least Figure 2 and as known to those skilled in the art based on the BLAST algorithm. *See Atschul, et al.* Claim 75 is amended to reflect 3 out of 9 amino acids being substituted or omitted as supported by the specification in at least Figure 2 and as known to those skilled in the art based on the BLAST algorithm. *See Atschul, et al.* Claim 76 is amended to reflect 2 out of 9 amino acids being substituted or omitted as supported by the specification in at least Figure 2 and as known to those skilled in the art based on the BLAST algorithm. *See Atschul, et al.* Claim 77 is amended to reflect at least 1 out of 9 amino acids being substituted or omitted as supported by the specification in at least Figure 2 and as known to those skilled in the art based on the BLAST algorithm. *See Atschul, et al.*

Claim 78 is amended as per the suggestions of Examiner. Newly added Claim 79 is added as a permutation of the suggestion of the Examiner for Claim 78. Both claims are supported in the specification on at least page 13. In complying with the Examiner’s

suggestions, Applicants believe the claims as newly amended and as newly added are supported by the specification, adds no new matter, and are in proper form for allowance. Applicants respectfully request that the Examiner withdraw his rejections for the foregoing reasons.

Rejections Under 35 U.S.C. § 112, second paragraph—Indefiniteness

The Examiner has rejected Claim 60 for indefiniteness. More specifically, the Examiner states that that the definition for “Hsp47-related polypeptide” “places so few limitations on the ‘Hsp47-related polypeptide’ of the claim that the metes and bounds of the claim cannot be known.

Applicants respectfully disagree. The term “Hsp47-related polypeptide” has definite meaning in the context of the present disclosure and the present invention. Nevertheless, to place the claims in better form for allowance, Applicants hereby amend claim 60 to include the phrase “a polypeptide that contains at least one sequence selected from the group comprising AX<sub>1</sub>X<sub>2</sub>X<sub>3</sub>AX<sub>4</sub>X<sub>5</sub>X<sub>6</sub>R, AX<sub>1</sub>LSAEX<sub>5</sub>X<sub>6</sub>R, AX<sub>1</sub>X<sub>2</sub>X<sub>3</sub>AEQLR, and AVLSAX<sub>4</sub>X<sub>5</sub>LR” which is supported in the specification on at least page 9. Applicants hereby amend dependent claims to claim 60—claims 61, 62, 63 and 65—to reflect the amendment of claim 60 by deleting the phrase “Hsp47-related.”

Rejections Under 35 U.S.C. § 102(b)

The Examiner has rejected claims 51 and 60-78 under 35 U.S.C. § 102(b) as being anticipated by Hoppe, et al. (1995). The Examiner particularly cites the last line of the abstract, which states, “The potential of p46 to prevent vascular leak syndrome associated with AI or CIK anti-tumor purging protocols is currently under investigation in a SCID/hu in-vivo model.”

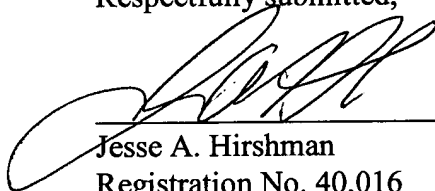
Applicants respectfully disagree with the Examiner. The cited reference does not teach each and every element of the claims. For example, the abstract does not teach a particular

amino acid sequence of a peptide, nor does it teach damage by lymphocytes, NK cells or NK-like cells. In addition, research has shown that the premise that CIK cells are associated with vascular leak syndrome is false. *See* Lu et al, J. Immunol. 153: 1687-1696 (1994) and Doctoral Thesis of Ernest G. Hope, "Heat Shock Protein 47 Mediated Response Modulation of Non-MCC I Restricted Cytotoxic T-Lymphocytes," pp. 95 and 96, June, 1999, UMI Number: 9958115 (provided herein with a Supplemental IDS.)

Notwithstanding the Examiner's rejection, the Applicants amend claim 51 to include damage caused by lymphocytes, NK cells or NK-like cells. In addition, Claims 80-292 are newly added and are supported at least by Figure 2 of the specification.

In light of the amendments and new claims, Applicants believe the claims are supported by the specification with no new matter added, and are in proper form for allowance. Applicants respectfully request that the Examiner withdraw his rejections for the foregoing reasons and allow pending claims 60-292.

Respectfully submitted,



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